

Genome mining indicates that the genus *Xanthomonas* is a promising reservoir for new bioactive non-ribosomally synthesized peptides

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Xanthomonas is a large genus of Gram-negative bacteria that cause disease in hundreds of plant species. To date, the only known small molecule synthesized by non-ribosomal peptide synthesis (NRPS) in this genus is albicidin produced by *Xanthomonas albilineans*. The DNA gyrase inhibitor albicidin is not only an important virulence factor but also a possible lead structure for novel antibiotics. This study aims to estimate the biosynthetic potential of *Xanthomonas* spp. by *in silico* analyses of NRPS genes with unknown function recently identified in the sequenced genomes of *X. albilineans* and related species of *Xanthomonas*. We performed *in silico* analyses of NRPS genes present in all published genome sequences of *Xanthomonas* spp., as well as in unpublished draft genome sequences of *Xanthomonas oryzae* pv. *oryzae* strain BAI3 and *Xanthomonas* spp. strain XaS3. The most unexpected result of these analyses is that these two latter strains, together with *X. albilineans* strain GPE PC73 and *X. oryzae* pv. *oryzae* strains X8-1A and X11-5A, possess novel NRPS gene clusters. Furthermore, these *Xanthomonas* spp. strains share related NRPS-associated genes such as those required for the biosynthesis of non-proteinogenic amino acids or for the secretion of peptides. *In silico* prediction of peptide structures according to the NRPS architecture accounts for eight different peptides, each specific to its producing strain. Interestingly, these eight peptides cannot be assigned to any known gene cluster or related to known compounds from natural product databases. PCR screening of a collection of 94 plant pathogenic bacteria indicates that these novel NRPS gene clusters are specific to the genus *Xanthomonas* and are also present in *Xanthomonas translucens* and *X. oryzae* pv. *oryzicola*. Further genome mining revealed (i) novel NRPS genes shared by *Xanthomonas* spp. strains GPE PC73 and XaS3 with the plant-associated bacterium *Bradyrhizobium* spp. strain BTAi and (ii) novel NRPS genes specific to *X. oryzae* pv. *oryzicola* or *Xanthomonas sacchari*. This study revealed the significant potential of the genus *Xanthomonas* of producing new non-ribosomally synthesized peptides. Interestingly, this biosynthetic potential seems to be specific to strains of *Xanthomonas* associated with monocotyledonous plants, suggesting a putative involvement of new non-ribosomally synthesized peptides in plant-bacteria interactions.